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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,378	10/05/2006	Masayo Takahashi	12480-000147/US	3138
30593 7590 08/17/2007 HARNESS, DICKEY & PIERCE, P.L.C. P.O. BOX 8910 RESTON, VA 20195			EXAMINER MACFARLANE, STACEY NEE	
			ART UNIT 1649	PAPER NUMBER
			MAIL DATE 08/17/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/551,378	Applicant(s) TAKAHASHI ET AL.	
	Examiner Stacey MacFarlane	Art Unit 1649	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 31 May 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3-8,11-13 and 17-19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-8, 11-13 and 17-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>3/15/2007</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### **Response to Amendment**

1. Claims 1, 3, 8 and 19 have been amended as requested in the amendment filed on May 31, 2007. Claims 2, 9-10 and 14-16 have been cancelled. Following the amendment, claims 1, 3-8, 11-13 and 17-19 are pending in the instant application.

Claims 1, 3-8, 11-13 and 17-19 are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's amendment necessitated new grounds of rejection set forth below.

### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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6. Claims 1, 3-8, 11-13 and 17-19, as currently amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawasaki et al. (*supra* and as cited in the previous Office Action mailed March 8, 2007), and further in view of Gospodarowicz et al. (cited in the previous Office Action). The amended Claim 1 is now drawn to a method of producing a lens cell comprising: an embryonic stem (ES) cell maintenance step of maintaining an ES cell by using a medium containing a fibroblast growth factor FGF-2 at a concentration of 2 ng/ml to 50 ng/ml; a washing step, carried out between the ES cell maintenance step and the differentiation inducing step, of washing the maintained ES cell only once with an ES differentiation medium; and a differentiation inducing step, carried out after the ES cell maintenance step, of inducing differentiation of the ES cell into a lens cell by implanting and culturing the ES cell on a mouse-skull-cell PA6 at a cell density of 2 colonies/cm<sup>2</sup> to 6.5 colonies/cm<sup>2</sup>.

The Kawasaki reference teaches a method of producing embryonic stem cell products comprising both a "maintenance" step and a "differentiation" step (pages 1580-1581). The maintenance step of the prior art teaches undifferentiated primate ES cells, derived from a primate, and specifically the cynomolgus monkey (line 1 of the Materials and Methods section of page 1580), were maintained with a medium containing 4 ng/ml basic fibroblast growth factor (paragraph bridging pages 1580-1581), then induced to differentiate using differentiation inducing medium (page 1581, lines 8-10).

It is common knowledge in the art that FGF-2 of the claim is equivalent to the "basic fibroblast growth factor" of the reference. As the Gospodarowicz reference teaches, fibroblast growth factor can be fractionated using acidic and basic pH

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producing two slightly different forms termed "acidic fibroblast growth factor" and "basic fibroblast growth factor", termed FGF-1 and FGF-2, respectively. Thus, the basic fibroblast growth factor of the reference teaches the FGF-2 of the claims.

The Kawasaki reference further teaches that the differentiation step comprises ES cells "plated on PA6 cells at a density of 500 clumps/10 cm dish" (page 1581, column 1, lines 8-10). The instant specification recites a "cell density of 2 to 6.5 (colonies/cm<sup>2</sup>) is equivalent to about 150 to 500 colonies when converted into the number of colonies per culture dish, 10 cm in diameter" (page 9, lines 1-4). Thus, for reasons of record, claims that recite the limitations of plating ES cells on PA6 cells at a density of "2.5 colonies/cm<sup>2</sup> to 6.5 colonies/cm<sup>2</sup>" (Claim 1) or "2.5 colonies/cm<sup>2</sup> to 4.0 colonies/cm<sup>2</sup>" (Claims 5, 12 and 13), are obvious over the Kawasaki reference. The medium defined as "differentiation medium" (Kawasaki, page 1581, column 1, lines 3-6) is the same medium in which the ES cells are cultured during the differentiation inducing step of the method (page 1581, column 1, lines 8-10).

The Kawasaki reference inherently teaches the product-by-process as claimed in the instant claims 8 and 19. Lens cells are inherent among the cells produced by the method. Section 2112.01 of the MPEP provides the guidance that when the structure in the reference is substantially identical to that of the claims and the products are produced by identical processes, then a *prima facie* case of obviousness has been established (See *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430,433. CCPA 1977).

The sole difference between the prior art and the instant claims is that the prior art recites a washing step carried out between maintenance and differentiation steps in

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which the undifferentiated ES cell colonies are washed twice with differentiation medium (page 1581, column 1, lines 2-6), whereas the amended instant claim recites that cells are washed "only once" (Claim 1).

The Kawasaki prior art teaches each element of the claimed method: maintenance step, washing step and differentiation step and one of ordinary skill in the art would have been able to perform the method using known methods, such as substituting only one wash for the two washes, with the predictable results of yielding the same product. In *KSR International Co. v. Teleflex, Inc.*, the Supreme Court has stated that where there is a "pressure to solve a problem and a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense" (*KSR International Co. v. Teleflex, Inc.* 127 S. Ct. 1727, 82 USPQ2d 1385, Supreme Court, April 30, 2007). In the instant case, the problem to be solved is the need for a wash between maintenance and differentiation steps. Examiner asserts that it is well within the technical grasp of a person of ordinary skill in the art to recognize that there are only a finite number of identified solutions - washing once or maybe twice, is sufficient. Thus, substitution of only one wash in place of the two as taught by the prior art, would be *prima facie* obvious to a skilled artisan. Furthermore, the KSR decision forecloses the argument that a **specific** teaching, suggestion, or motivation is required to support a finding of obviousness, as suggested by Applicant in Remarks filed May 31, 2007 (page

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6, last line). For further reference, see the recent Board decision *Ex parte Smith*, USPQ2d, Bd. Pat. Appl. & Interf. June 25, 2007, which cites *KSR*, 82 USPQ2d at 1396.

Therefore, Claims 1, 3-8, 11-13 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawasaki et al. (*supra*) as the invention as a whole is *prima facie* obvious, if not actually anticipated by the reference.

### ***Conclusion***

7. No Claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on Monday-Thursday 6:30AM-4:00 PM & ALT. Fridays, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane  
Examiner  
Art Unit 1649

SNM

  
OLGA N. CHERNYSHEVA, Ph.D.  
PRIMARY EXAMINER